

**PATENT**

**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

Applicants:	Bryan, <i>et al.</i>	
Serial No.:	10/594,064 - Case No.: 21571P	Art Unit: 1656
Patent No.	7,700,103	
Filed:	September 25, 2006	Examiner: K.H. Gebreyesus
For:	OPTIMIZED EXPRESSION OF HPV 52 L1 IN YEAST	

Commissioner for Patents  
PO Box 1450  
Alexandria, VA 22313-1450

**APPLICATION FOR PATENT TERM ADJUSTMENT UNDER 37 C.F.R. §1.705(d)**

Sir:

This is a request for reconsideration of the patent term adjustment (PTA) indicated in the Issue Notification mailed March 31, 2010 and noted on the front page of the corresponding granted patent (US 7,700,103). This request is submitted within two months of the date of patent issuance on April 20, 2010. The patent that issued from the subject application, US Patent 7,700,103, is not subject to a terminal disclaimer.

The Commissioner is authorized to charge the fee set forth in 37 C.F.R. §1.18(e) to Deposit Account No. 13-2755. Please charge any fee deficiencies in connection with this request to Deposit Account No. 13-2755.

Applicants respectfully request that the PTA determination be revised to include the correct number of days accrued pursuant to 37 C.F.R. § 1.702(a) "*Failure to take certain actions within specified time frames,*" and § 1.702(b) "*Failure to issue a patent within three years of the actual filing date of the application.*" Applicants submit that there was 499 days of Patent Office delay under 1.702(a). Additionally, there were 207 days of Patent Office delay under 1.702(b), which occurred more than three years after the subject application was filed and does not overlap with the 499 days of Patent Office delay due under 37 C.F.R. § 1.702(a). There were no instances in which Applicants failed to engage in reasonable efforts to conclude processing or examination of the application. Accordingly, Applicants are entitled to  $499 + 207 = 706$  days of PTA.

**PTA under 37 C.F.R. § 1.702(a):**

According to 37 C.F.R. § 1.702(a)(1), the term of an original patent shall be adjusted if the issuance of the patent was delayed due to the failure of the Office to mail at least one of a notification under 35 U.S.C. § 132 or a Notice Of Allowance under 35 U.S.C. § 151 not later

than fourteen months after the date on which the application fulfilled the requirements of 35 U.S.C. § 371 in an international application. The requirements under section 371 for this international application were fulfilled on September 25, 2006. The date fourteen months after the section 371 requirements were fulfilled is November 25, 2007. A Restriction Requirement was mailed on April 7, 2009, which constitutes 499 days of Patent Office delay under 37 C.F.R. § 1.703(a); i.e., the number of days from November 25, 2007 to April 7, 2009.

The PTA determination of the Patent Office (copy attached hereto as "Exhibit A") lists 499 days of Patent Office delay under 37 C.F.R. § 1.702(a), 207 days of Patent Office delay under 37 C.F.R. § 1.702(b), and 120 days of alleged Applicant delay, resulting in a total of 586 days of PTA. The 120 period which constitutes the alleged "Failure of the Applicant to Engage in Reasonable Efforts to Conclude Processing or Examination of the Application" (alleged Applicant delay) appears to begin from Applicants' response to the Restriction Requirement on May 5, 2009 and ends with an amendment made by the Office to Figure 1B on August 20, 2009 (labeled "Workflow – Drawings Finished" on the Patent Term Adjustment History). The specific amendment, which was made one month after mailing of the Notice of Allowance on July 20, 2009, consisted of changing the label "FIG. 1A," which erroneously appeared on the first two sheets of Figure 1, to "FIG 1B."

Applicants respectfully assert that the noted amendment to the Drawings does not constitute a "failure of the applicants to engage in reasonable efforts to conclude processing or examination of the application." The amendment to FIG 1B was made on the initiative of the Office after the application was allowed and was not objected to at any point during the prosecution of the present application. Specifically, the Restriction Requirement that was mailed on April 7, 2009, did not contain any mention of the error to Figure 1B, nor did it present an objection to the Figures at all (see copy of Restriction Requirement, attached as "Exhibit B"). Thus, Applicants provided a complete response to the Restriction Requirement on May 5, 2009. There was no further communication from the Office which the Applicants failed to respond to in a timely manner. For this reason, Applicants did not fail to engage in reasonable efforts to conclude processing or examination of the application as set forth in 37 C.F.R. § 1.704. Accordingly, the PTA accrued under 37 C.F.R. § 1.702(a)(1) is PTO Delay – Applicant Delay =  $499 - 0 = 499$  days.

PTA under 37 C.F.R. § 1.702(b):

According to 37 C.F.R. § 1.702(b), the term of the original patent shall be adjusted if the issuance of the patent was delayed due to the failure of the Office to issue a patent within three years after the date on which the national stage commenced under 35 U.S.C. § 371. The date three years after commencement of the national stage is September 25, 2009. According to 37 C.F.R. § 1.703(b), the number of days accrued under Rule 1.702(b) is 207 days; i.e., the number of days from September 25, 2009 to patent grant on April 20, 2010.

There has been no delay due to Applicants during the 1.703(b) period. Accordingly, Applicants are entitled to  $499 + 207 = 706$  days of PTA.

Summary:

It is respectfully requested that the PTA determination for U.S. patent 7,700,103 be revised to reflect that there was no Applicant delay in the prosecution of the present application. The proper PTA should be 706 days, which is 499 days of Patent Office delay for failure to issue a Restriction Requirement within fourteen months after the date on which the application fulfilled the requirements of 35 U.S.C. § 371, plus 207 days of Patent Office delay for failure to issue a patent within three years.

Respectfully submitted,

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Date: April 27, 2010

10/594.064

OPTIMIZED EXPRESSION OF HPV 52 L1 IN YEAST

04-20-

2010::11:20:29

**Patent Term Adjustments**

Patent Term Adjustment (PTA) for Application Number: 10/594,064

Filing or 371(c) Date:	09-25-2006	USPTO Delay (PTO) Delay (days):	-
Issue Date of Patent:	04-20-2010	Three Years:	-
Pre-Issue Petitions (days):	-	Applicant Delay (APPL) Delay (days):	-
Post-Issue Petitions (days):	-	Total PTA (days):	586
USPTO Adjustment(days):	-	Explanation Of Calculations	

**Patent Term Adjustment History**

Date	Contents Description	PTO(Days)	APPL(Days)
04-20-2010	PTA 36 Months	207	
04-20-2010	Patent Issue Date Used in PTA Calculation		
03-23-2010	Dispatch to FDC	↑	
03-15-2010	Mail-Petition Decision - Dismissed	↑	
03-15-2010	Petition Decision - Dismissed	↑	
10-20-2009	Application Is Considered Ready for Issue	↑	
10-19-2009	Issue Fee Payment Verified	↑	
10-19-2009	Petition Entered	↑	
10-19-2009	Issue Fee Payment Received	↑	
08-20-2009	Workflow - Drawings Finished		120
08-20-2009	TC Return to Pubs		↑
08-10-2009	Sequence Forwarded to Pubs on Tape		↑
07-20-2009	Mail Notice of Allowance		↑
07-17-2009	Document Verification		↑
07-17-2009	Notice of Allowance Data Verification Completed		↑
07-17-2009	Examiner's Amendment Communication		↑
07-05-2007	Information Disclosure Statement considered		↑
09-25-2006	Information Disclosure Statement considered		↑
06-17-2009	Date Forwarded to Examiner		↑
05-05-2009	Response to Election / Restriction Filed		↑
04-07-2009	Mail Restriction Requirement	499	
04-03-2009	Requirement for Restriction / Election	↑	
09-18-2008	PG-Pub Issue Notification	↑	
08-04-2008	Case Docketed to Examiner in GAU	↑	
07-29-2008	Filing Receipt - Corrected	↑	
07-28-2008	IFW TSS Processing by Tech Center Complete	↑	
07-05-2007	Information Disclosure Statement (IDS) Filed	↑	
09-25-2006	Request for Foreign Priority (Priority Papers May Be Included)	↑	
09-25-2006	Reference capture on IDS	↑	
09-25-2006	Preliminary Amendment	↑	
09-25-2006	Information Disclosure Statement (IDS) Filed	↑	
06-20-2008	Application Dispatched from OIPE	↑	
09-25-2006	371 Completion Date	↑	
06-11-2008	Sent to Classification Contractor		

06-11-2008	Filing Receipt		
06-11-2008	Notice of DO/EO Acceptance Mailed		
07-05-2007	Information Disclosure Statement (IDS) Filed		
10-12-2006	Cleared by OIPE CSR		
10-06-2006	CRF Is Good Technically / Entered into Database		
09-25-2006	CRF Disk Has Been Received by Preexam / Group / PCT		
09-25-2006	Initial Exam Team nn		

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**EXHIBIT B****UNITED STATES PATENT AND TRADEMARK OFFICE**

UNITED STATES DEPARTMENT OF COMMERCE  
United States Patent and Trademark Office  
Address: COMMISSIONER FOR PATENTS  
P.O. Box 1450  
Alexandria, Virginia 22313-1450  
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/594,064	09/25/2006	Janine T. Bryan	21571P	5405
210 7590 04/07/2009 MERCK AND CO., INC P O BOX 2000 RAHWAY, NJ 07065-0907			EXAMINER GEBREYESUS, KAGNEW H	
			ART UNIT 1656	PAPER NUMBER
			MAIL DATE 04/07/2009	DELIVERY MODE PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b> 10/594,064	<b>Applicant(s)</b> BRYAN ET AL.	
	<b>Examiner</b> KAGNEW H. GEBREYESUS	<b>Art Unit</b> 1656	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

#### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 1 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) ☒ Responsive to communication(s) filed on 03 July 2008.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) ☒ Claim(s) 1-28 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☐ Claim(s) \_\_\_\_\_ is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☒ Claim(s) 1-28 are subject to restriction and/or election requirement.

#### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)          | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____                                      |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)          | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____  | 6) <input type="checkbox"/> Other: _____                          |

## **DETAILED ACTION**

### ***Election/Restrictions***

Restriction is required under 35 U.S.C. 121 and 372.

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1.

In accordance with 37 CFR 1.499, applicant is required, in reply to this action, to elect a single invention to which the claims must be restricted.

Group I, claim(s) 1-7 are drawn to A nucleic acid molecule comprising a sequence of nucleotides that encodes an HPV52 L1 protein as set forth in SEQ ID NO:2, the nucleic acid sequence being codon-optimized for high-level expression in a yeast cell, vector and host cell comprising the nucleic acid

Group II, claim(s) claims 8-15, 17-23, 25 and 27 drawn to virus-like particles (VLPs) comprised of recombinant L1 protein of HPV52, wherein the recombinant L1 protein is produced in yeast.

Group III, claims 8-15, 17-23, 25 and 27 or drawn to virus-like particles (VLPs) comprised of recombinant L1 +L2 protein of HPV52, wherein the recombinant L1 + L2 proteins are produced in yeast.



The technical feature linking the invention first claimed is a codon optimized DNA construct that encodes an HPV 52 protein. However this technical feature is not a special technical feature because of the combined teaches of US 5,643,715 Lancaster et al Sharp et al (1991) and Hofmann et al (1995). US 5,643,715 Lancaster et al teach an isolated nucleic acid molecule comprising a sequence of nucleotides that encodes an HPV52 L1 protein. Furthermore they teach that cloning vectors comprising HPV 52 DNA or fragments can be expressed in bacterial or eukaryotic host cells. (See column 6 last paragraph).

Sharp et al (1991) teach different degrees of codon usage in *Saccharomyces cerevisiae* from which an optimal codon for expression in *Saccharomyces cerevisiae* can be selected (see table 2 on page 673).

Hofmann et al (1995) teach that the major (L1) and minor (L2) proteins of HPV proteins are promising candidate targets for producing vaccines (immunoprophylaxis). They further teach that the *Saccharomyces cerevisiae* yeast expression system exhibits many advantages for the development of vaccine. Hofmann et al do not teach expressing HPV52 from codon optimized the HPV52 DNA.

Thus it would have been obvious for one of ordinary skill in the art to use *Saccharomyces cerevisiae* to express the HPV 52 L1 and L1+L2 genes in *Saccharomyces cerevisiae* for the many advantages discussed in Hofmann et al. They teach that yeast have the potential to produce large quantities of proteins in their native conformation; it has the apparatus for some post translational modifications similar to those of mammalian cells and that yeast derived products for human use have been

accepted from the regulatory standpoint. They further teach production of VLPs from HPV6a L1 and L1+L2 in yeast. (see page 507 1<sup>st</sup> paragraph). Thus following this model an ordinary skill in the art would be motivated to produce VLPs from HPV52 L1 and L1+L2 vaccine in *Saccharomyces cerevisiae*. This is because HPV 52 is one among many human papillomaviruses (HPV) serotypes that known to be associated with disease (see for example Zhao et al (US 6,436,402) column 3 lines 29-40). Therefore the technical feature linking the invention of group I and II is not a special technical feature as it does not contribute over the prior art as required in PCT rule 13.2.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to KAGNEW H. GEBREYESUS whose telephone number is (571)272-2937. The examiner can normally be reached on 8:30am-5:30pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jon Weber can be reached on 571-272-0925. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Art Unit: 1656

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Kagnew H Gebreyesus/  
Examiner, Art Unit 1656  
4/1/2009

/JON P WEBER/  
Supervisory Patent Examiner, Art Unit 1657